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individuals.

10. The method of claim 5, wherein said population comprises a population of patients having subcutaneous nodules.

11. The method of claim 5, wherein said population comprises a population of patients having extra-articular involvement.

12. The method of claim 5, wherein said population comprises a population of patients having major joint destruction.

13. A method for determining the predisposition of a rheumatoid arthritis patient to develop severe disease, said method comprising:

a) determining the level of a cytokine within a sample from said patient,  
b) determining the frequency of CD4<sup>+</sup>/CD28<sup>null</sup> cells in said patient,  
c) comparing said level of said cytokine to a reference level and said frequency of CD4<sup>+</sup>/CD28<sup>null</sup> cells to a reference frequency to obtain information about said predisposition, and

d) determining if said patient is predisposed to develop severe disease based on said information.

14. The method of claim 13, wherein said cytokine comprises a cytokine selected from the group consisting of IL-4, IL-10, and IFN- $\gamma$ .

15. The method of claim 13, wherein said sample comprises a tissue biopsy.

16. The method of claim 15, wherein said tissue biopsy comprises a synovial tissue biopsy.

17. The method of claim 13, wherein said reference level comprises the median level of

cytokine found in tissue samples derived from a population.

18. The method of claim 17, wherein said population comprises a population of patients having a diffuse rheumatoid arthritis condition.
19. The method of claim 17, wherein said population comprises a population of patients having a follicular rheumatoid arthritis condition.
20. The method of claim 17, wherein said population comprises a population of patients having a granulomatous rheumatoid arthritis condition.
21. The method of claim 17, wherein said population comprises a population of healthy individuals.
22. The method of claim 17, wherein said population comprises a population of patients having subcutaneous nodules.
23. The method of claim 17, wherein said population comprises a population of patients having extra-articular involvement.
24. The method of claim 17, wherein said population comprises a population of patients having major joint destruction.
25. The method of claim 13, wherein said frequency of CD4<sup>+</sup>/CD28<sup>null</sup> cells comprises the percent of CD4<sup>+</sup> cells that are CD28 negative.
26. The method of claim 25, wherein said reference frequency is derived from the CD4<sup>+</sup>/CD28<sup>null</sup> cell frequency from a population.
27. A method for determining the predisposition of a rheumatoid arthritis patient to

[illegible]

28. The method of claim 27, wherein said cytokine comprises a cytokine selected from the group consisting of IL-4, IL-10, and IFN- $\gamma$ .

30. The method of claim 27, wherein said tissue biopsy comprises a synovial tissue biopsy.

31. The method of claim 27, wherein said reference level comprises the median level of cytokine found in tissue samples derived from a population.

32. The method of claim 31, wherein said population comprises a population of patients having a diffuse rheumatoid arthritis condition.

33. The method of claim 31, wherein said population comprises a population of patients having a follicular rheumatoid arthritis condition.

34. The method of claim 31, wherein said population comprises a population of patients having a granulomatous rheumatoid arthritis condition.

35. The method of claim 31, wherein said population comprises a population of healthy

individuals.

36. The method of claim 31, wherein said population comprises a population of patients having subcutaneous nodules.

37. The method of claim 31, wherein said population comprises a population of patients having extra-articular involvement.

38. The method of claim 31, wherein said population comprises a population of patients having major joint destruction.

39. The method of claim 27, wherein said polymorphism comprises an HLA-DRB1 allele that encodes a polypeptide having an uncharged amino acid at position 74.

40. The method of claim 39, wherein said polymorphism comprises an HLA-DRB1 allele that encodes a polypeptide free from negatively charged amino acids at positions 70 and 71.

41. A method for determining the predisposition of a rheumatoid arthritis patient to develop severe disease, said method comprising:

- a) determining the level of a cytokine within a sample from said patient,
- b) determining the frequency of CD4<sup>+</sup>/CD28<sup>null</sup> cells in said patient,
- c) comparing said level of said cytokine to a reference level and said frequency of CD4<sup>+</sup>/CD28<sup>null</sup> cells to a reference frequency to obtain information about said rheumatoid arthritis condition,
- d) determining the presence of a polymorphism in an HLA-DRB1 allele in said patient, and
- e) determining if said patient is predisposed to develop severe disease based on said information and said presence of said polymorphism.

42. A kit for providing diagnostic information about a rheumatoid arthritis condition in a

patient, said kit comprising:

a) a binding pair member, wherein said binding pair member has specific binding affinity for a cytokine such that the level of said cytokine within a sample from said patient is determinable, and

b) a reference chart, wherein said reference chart contains information about cytokine levels such that an indication of the diffuse, follicular, or granulomatous nature of said rheumatoid arthritis condition is determinable based on said level of said cytokine within said sample.

43. A kit for providing diagnostic information about a rheumatoid arthritis condition in a patient, said kit comprising:

a) a binding pair member, wherein said binding pair member has specific binding affinity for a nucleic acid sequence encoding a cytokine such that the level of said cytokine within a sample from said patient is determinable, and

b) a reference chart, wherein said reference chart contains information about cytokine levels such that an indication of the diffuse, follicular, or granulomatous nature of said rheumatoid arthritis condition is determinable based on said level of said cytokine within said sample.

44. A kit for determining the predisposition of a rheumatoid arthritis patient to develop severe disease, said kit comprising:

a) a first binding pair member, wherein said first binding pair member has specific binding affinity for a cytokine or nucleic acid encoding said cytokine such that the level of said cytokine within a sample from said patient is determinable,

b) second binding pair member, wherein said second binding pair member has specific binding affinity for a  $CD4^+/CD28^{null}$  cell marker such that the frequency of  $CD4^+/CD28^{null}$  cells in said patient is determinable, and

c) a reference chart, wherein said reference chart contains information about cytokine levels and  $CD4^+/CD28^{null}$  cell frequencies such that an indication of said predisposition is determinable based on said level of said cytokine within said sample and said frequency of

CD4<sup>+</sup>/CD28<sup>null</sup> cells in said patient.

45. A kit for determining the predisposition of a rheumatoid arthritis patient to develop severe disease, said kit comprising:

- a) a binding pair member, wherein said binding pair member has specific binding affinity for a cytokine or nucleic acid encoding said cytokine such that the level of said cytokine within a sample from said patient is determinable,
- b) an oligonucleotide primer, wherein said oligonucleotide primer has specific binding affinity for at least a portion of the locus containing an HLA-DRB1 allele such that a polymorphism of HLA-DRB1 allele in said patient is determinable, and
- c) a reference chart, wherein said reference chart contains information about cytokine levels such that an indication of said predisposition is determinable based on said level of said cytokine within said sample and said polymorphism of said patient.

46. The kit of claim 45, wherein said kit comprises a plurality of said oligonucleotide primers.

47. A kit for determining the predisposition of a rheumatoid arthritis patient to develop severe disease, said kit comprising:

- a) a first binding pair member, wherein said first binding pair member has specific binding affinity for a cytokine or nucleic acid encoding said cytokine such that the level of said cytokine within a sample from said patient is determinable,
- b) a second binding pair member, wherein said second binding pair member has specific binding affinity for a CD4<sup>+</sup>/CD28<sup>null</sup> cell marker such that the frequency of CD4<sup>+</sup>/CD28<sup>null</sup> cells in said patient is determinable,
- c) an oligonucleotide primer, wherein said oligonucleotide primer has specific binding affinity for at least a portion of the locus containing an HLA-DRB1 allele such that the a polymorphism of said HLA-DRB1 allele in said patient is determinable, and
- d) a reference chart, wherein said reference chart contains information about cytokine levels and CD4<sup>+</sup>/CD28<sup>null</sup> cell frequencies such that an indication of said predisposition is

determinable based on said level of said cytokine within said sample, said frequency of CD4<sup>+</sup>/CD28<sup>null</sup> cells in said patient, and said polymorphism of said HLA-DRB1 allele.

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